Background. In sickle cell disease (SCD), there is a high incidence of silent cerebral infarction (SCI) that peaks in childhood\(^1\), frequently seen as small, focal lesions in deep white matter or basal ganglia\(^2\). Recent research has shown cortical volumetric differences in those with high- and low-IQ\(^3\) and cortical thinning\(^4\), but only one study reports significant reduction in volume of subcortical grey matter\(^5\). SCD has been described as a state of chronic hypoxia\(^6\), and some subcortical structures, such as the hippocampus, may be particularly vulnerable.

Methods. We acquired retrospective data from an East London cohort of children with SCD: a total of 33 patients and 21 controls (10 sibling controls). MRI was performed on a 1.5T Siemens Vision system and all subjects had FLASH 3D T1-weighted volumes (0.8mm x 0.8mm x 1mm). The patients were categorized into two groups based on presence of an SCI and classified as lesion patients (SCD+L; n=15, 7M, mean age= 18.9 years), no lesion patients (SCD-L; n=18, 12M, mean age=17.5 years) and controls (n=21, 7M, mean age=17.3 years). Subcortical structure segmentations were analyzed using Freesurfer v5.1, with each subject's subcortical volumes represented as a percentage of his/her own intracranial volume. An analysis of covariance was performed to control for age against subcortical volume variables in the three groups, and the Tukey-Kramer method was used to perform post-hoc tests to determine which groups' means were significantly different from each other.

Results.

Results for subcortical volumes are summarized in Figure 1. The volumes of the palladium, hippocampus, amygdala and cerebellar cortex were significantly reduced bilaterally, with the greatest reduction in SCD+L group, followed by SCD-L, compared to Controls. The most highly significant volumetric differences were found in the amygdala bilaterally, right cerebellar cortex and right putamen, with post-hoc tests showing all differences were driven by a highly significant difference between Controls and SCD+L.

Conclusion. This study is the first to our knowledge to specifically investigate volumes of subcortical structures in patients with SCD, with and without SCI. One previous report found volumetric decreases in central grey matter; however the present study found specific significant decreases bilaterally in the hippocampus, amygdala, cerebellar cortex, pallidum, and right-hemisphere thalamus, caudate, and putamen, as well as total subcortical grey matter volume. Our findings provide further evidence to support the hypothesis that chronic hypoxia may be the underlying cause of growth delay\(^5\) as volumetric deficits are seen in patients without visible lesions compared to age- and race-matched controls, and consistent with the picture of a global diffuse pattern of brain injury.

References.